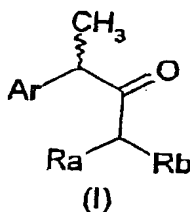


Amended

CLAIMS

1. Use of (*R,S*)-1-Arylethylketone compounds of formula I and their single (*R*) and (*S*) enantiomers:



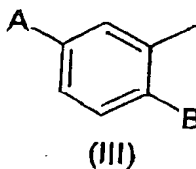
wherein:

- Ar represents phenyl, optionally substituted by one to three substituents, which are the same or different from one another, selected from:

halogens, C₁-C₄-alkyl, C₁-C₄-alkoxy, hydroxy, C₁-C₄-acyloxy, phenoxy, cyano, nitro, amino, C₁-C₄-acylamino, halogen-C₁-C₃-alkyl, halogen C₁-C₃-alkoxy, benzoyl;

or Ar represents 4-thienoyl-phenyl, 4-(1-oxo-2-isoindoliny)-phenyl, 3-chloro-4-(2,5-dihydro-1H-pyrrol-1-yl)phenyl, 6-methoxy-β-naphthyl, 1-hydroxy-phenyl-1-methyl;

or Ar represents a residue of formula III:



wherein A is benzyl, phenoxy, benzoyl, benzoyloxime, 1-hydroxy-phenyl-1-methyl, B is hydroxy, C₁-C₄-acyloxy or a group of formula -O-C(=S)-N(CH₃)₂, or -S-C(=O)-N(CH₃)₂;

- Ra and Rb are independently chosen in the group of hydrogen, linear or branched C₁-C₆ alkyl, phenyl, α- or β-naphthyl, 2, 3, 4-pyridyl, C₁-C₄-alkylphenyl, C₁-C₄-alkyl(α- or β-naphthyl), C₁-C₄-alkyl(2, 3, 4-pyridyl), cyano (-CN), carboxamide, carboxyl or carboxyesters of formula CO₂R" wherein R" is the residue of a linear or

(4x50 mL). The organic extracts are dried on sodium sulfate; after evaporation of the solvent, the residue is purified on silica gel, eluted with AcOEt to yield, as a colourless oil, 3.02 g of (R) (-)-dimethyl 3-(4-isobutyl)-2-oxobutan-1-phosphonate.

$[\alpha]_D = -171^\circ$ ($c=1$; CH₃OH); ¹H-NMR (CDCl₃): δ 7.03 (s, 4H); 4.1-3.9 (dd, 2H, $J_1=15\text{Hz}$, $J_2=8\text{Hz}$); 3.8 (s, 3H); 3.70 (m, 1H); 3.65 (s, 3H); 2.55 (d, 2H, $J=8\text{Hz}$); 1.75 (m, 1H); 1.50 (d, 3H, $J=8\text{Hz}$); 0.85 (d, 6H, $J=7\text{Hz}$).

Example 7

(R) (-) 2-(4-isobutylphenyl)-7-*tert*-butoxycarbonylamino-heptan-3-one.

A solution of ethyl 5-*tert*-butoxycarbonylamino-2-ethoxycarbonyl-pentanoate (WO 94/10127) (1.59 g) in 3 mL of methanol is added to 8 mL of a 0.63 N solution of LiOH.H₂O in water/methanol (1:1); the mixture is stirred for 12 h at room temperature. The mixture is diluted with 10 mL of a saturated solution of monosodium phosphate, and the excess of methanol is removed under vacuum. The mixture is extracted with ethyl acetate (2x10 mL); from the organic extracts, combined and dried on sodium sulfate, by evaporation of the solvent 1.4 g (4.8 mmol) of 5-*tert*-butoxycarbonylamino-2-ethoxycarbonyl-pentanoic acid are obtained.

To a solution of the acid (2.4 mmol) in 8 mL of anhydrous THF 0.27 g (2.4 mmol) of commercially available magnesium ethylate is then added, and the suspension is stirred at room temperature up to complete dissolution of the reagents to form the magnesium complex.

Then a solution of 0.3 g of (R) (-) 2-(4'-isobutylphenyl)-propionylimidazolide is added, and the mixture is stirred for 4 h at room temperature. The mixture is acidified by addition of a few mL of 50% aqueous AcOH, and the solvent is evaporated under vacuum. The residue is repartitioned between water and ethyl acetate to yield, after the usual processing, crude product (0.42 g) of ethyl (R,S)-2-[R-2-(4-isobutyl)-propionyl]-5-*tert*-butoxycarbonylamino-pentanoate, which is purified by flash chromatography.

A solution of 0.15 g of β -ketoester in DMSO/NaCl/H₂O is then dealkoxydecarboxylated by heating to 135-145°C to yield 0.08 g of (R) (-) 2-(4-isobutylphenyl)-7-*tert*-butoxycarbonylamino-heptan-3-one.

$[\alpha]_D = -25$ ($c=1$; CH₃OH); ¹H-NMR (CDCl₃): δ 7.25 (s, 4H); 6.35 (bs, 1H, CONH); 3.70 (q, 1H, $J=8\text{Hz}$); 3.40 (m, 2H); 2.45 (d, 2H, $J=7\text{Hz}$); 2.31 (m, 2H); 1.85 (m, 1H); 1.75-1.62 (m, 4H); 1.60 (d, 3H, $J=7\text{Hz}$); 1.45 (s, 9H); 0.94 (d, 6H, $J=7\text{Hz}$).

Example 8

Following the procedure of Example 7, but using as a starting material a monoester of a substituted malonic acid chosen in the group of:

methyl 2-carboxy-propionate;

5 methyl 2-carboxy-2-phenyl acetate;

methyl 2-carboxy-3-phenyl propionate;

methyl 2-carboxy-3-(pyrid-3-yl) propionate;

methyl 2-carboxy-3-cyclopentyl propionate;

the following β -ketoesters were obtained:

10 methyl(R', S')-2-[R-2-(4-isobutylphenyl)-propionyl] propionate;

methyl(R', S')-2-[R-2-(4-isobutylphenyl)-propionyl]-2-phenyl acetate;

methyl(R', S')-2-[R-2-(4-isobutylphenyl)-propionyl]-3-phenyl propionate;

methyl(R', S')-2-[R-2-(4-isobutylphenyl)-propionyl]-3-(pyrid-3-yl) propionate;

methyl(R', S')-2-[R-2-(4-isobutylphenyl)-propionyl]-3-cyclopentyl propionate;

15 to obtain, after decarboxylation in DMSO/NaCl, the corresponding ketones:

R(-) 2-(4-isobutylphenyl)-pentan-3-one

$[\alpha]_D = -36$ (c=1; CH₃OH); ¹H-NMR (CDCl₃); δ 7.20 (d, 2H, J=7Hz); 7.10 (d, 2H, J=7Hz); 3.70 (q, 1H, J=8Hz); 2.47 (d, 2H, J=7Hz); 2.40 (q, 2H, J=7Hz); 1.82 (m, 1H); 1.55 (d, 3H, J=7Hz); 0.98 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

20 R(-) 2-(4-isobutylphenyl)-4-phenyl-butan-3-one

$[\alpha]_D = -48.5$ (c=1; CH₃OH); ¹H-NMR (CDCl₃); δ 7.35-7.18 (m, 5H); 7.15 (d, 2H, J=7Hz); 7.05 (d, 2H, J=7Hz); 3.72 (q, 1H, J=8Hz); 3.65 (s, 2H); 2.42 (d, 2H, J=7Hz); 1.80 (m, 1H); 1.60 (d, 3H, J=7Hz); 0.93 (d, 6H, J=7Hz).

R(-) 2-(4-isobutylphenyl)-5-phenyl-pentan-3-one

25 $[\alpha]_D = -40$ (c=1.5; CH₃OH); ¹H-NMR (CDCl₃); δ 7.37-7.20 (m, 5H); 7.10 (d, 2H, J=7Hz); 7.00 (d, 2H, J=7Hz); 3.70 (q, 1H, J=8Hz); 2.88 (m, 2H); 2.75 (m, 2H); 2.45 (d, 2H, J=7Hz); 1.82 (m, 1H); 1.63 (d, 3H, J=7Hz); 0.95 (d, 6H, J=7Hz). R(-) 2-(4-isobutylphenyl)-5-(pyrid-3-yl)-pentan-3-one

30 $[\alpha]_D = -89$ (c=1; CH₃OH); ¹H-NMR (CDCl₃); δ 8.62 (m, 2H); 7.80 (m, 1H); 7.35 (m, 1H); 7.15 (d, 2H, J=7Hz); 7.08 (d, 2H, J=7Hz); 5.35 (t, 2H, J=8Hz); 5.05 (t, 2H, J=8Hz); 3.72 (q, 1H, J=8Hz); 2.42 (d, 2H, J=7Hz); 1.80 (m, 1H); 1.63 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

Example 9

(R,S) 1-phenyl-4-(4'-isobutylphenyl)-1, 3-pentadione

A suspension of 0.55g of magnesium ethylate in a solution of 1.61g of benzoylacetic acid is stirred at room temperature, in an inert-gas atmosphere, up to total dissolution of the reagents. A solution of 0.6g of (R,S)-2-(4'-isobutylphenyl)-propionylimidazolide is added, and stirring is continued overnight at room temperature. The mixture is brought to neutrality by addition of a few drops of 50% aqueous AcOH, and is then evaporated to dryness under vacuum. The residue is repartitioned between water and ethyl acetate. The combined organic phases are dried on sodium sulfate, and evaporated to dryness. The residue is purified by flash chromatography to obtain 0.78g of (R,S) 1-phenyl-4-(4'-isobutylphenyl)-1, 3-pentadione.

¹H-NMR (CDCl₃); δ 7.90 (m, 2H); 7.65 (m, 1H); 7.52 (m, 2H); 7.20 (d, 2H, J=7Hz); 7.12 (d, 2H, J=7Hz); 3.77 (s, 2H); 3.68 (q, 1H, J=8Hz); 2.41 (d, 2H, J=7Hz); 1.82 (m, 1H); 1.60 (d, 3H, J=7Hz); 0.95 (d, 6H, J=7Hz).

Example 10

Following the procedure of Example 9, and using a β-ketoacid chosen in the group of acetylacetic acid, 4-phenyl-3-oxo-butyrric acid or nicotinoylacetic acid, in place of benzoylacetic acid, the following are obtained:

(R,S) 5-(4'-isobutylphenyl)-hexan-2, 4-dione

¹H-NMR (CDCl₃); δ 7.20 (d, 2H, J=7Hz); 7.12 (d, 2H, J=7Hz); 3.75 (s, 2H); 3.65 (q, 1H, J=8Hz); 2.40 (d, 2H, J=7Hz); 2.10 (s, 3H); 1.82 (m, 1H); 1.62 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

(R,S) 1-phenyl-5-(4'-isobutylphenyl)-2, 4-hexandione

¹H-NMR (CDCl₃); δ 7.35-7.20 (m, 5H); 7.15 (d, 2H, J=7Hz); 7.05 (d, 2H, J=7Hz); 3.75 (s, 2H); 3.68 (q, 1H, J=8Hz); 3.63 (s, 2H); 2.41 (d, 2H, J=7Hz); 1.80 (m, 1H); 1.64 (d, 3H, J=7Hz); 0.95 (d, 6H, J=7Hz).

(R,S) 1-(pyrid-2-yl)-4-(4'-isobutylphenyl)-1, 3-pentadione

¹H-NMR (CDCl₃); δ 8.60 (m, 2H); 7.81 (m, 1H); 7.37 (m, 1H); 7.18 (d, 2H, J=7Hz); 7.10 (d, 2H, J=7Hz); 3.70 (q, 1H, J=8Hz); 3.65 (s, 2H); 2.40 (d, 2H, J=7Hz); 1.81 (m, 1H); 1.65 (d, 3H, J=7Hz); 0.95 (d, 6H, J=7Hz).

Example 11

(R,S) 2-(4'-isobutylphenyl)-3-oxo-butyl, methyl-sulfoxide

A solution of sodium hydride (21 mmol) in dry methylsulfoxide (5 mL) is heated at 60°C, in an inert-gas atmosphere, for 1 h. A solution of 2.2 g (10 mmol) of methyl 2-(4'-isobutylphenyl)-propionate in dry methylsulfoxide is dropped, and stirring is continued for 2 h at 60 °C. The mixture is cooled at room temperature, brought to neutrality by addition of AcOH (0.25 mL), and diluted with diethyl ether. 1N HCl is added until pH=2 and CH₂Cl₂ and water are added. The two phases are debated and separated; the combined organic phases are dried on sodium sulfate, and evaporated to dryness. The residue is purified by flash chromatography to obtain 0.350 g of (R,S) 2-(4'-isobutylphenyl)-3-oxo-butyl, methyl-sulfoxide.

¹H-NMR (CDCl₃); δ 7.14 (s, 4H); 3.85 (m, 2H); 3.52 (m, 1H); 2.65 + 2.54 (s, 3H); 2.47 (d, 2H, J=7Hz); 1.87 (m, 1H); 1.43 (d, 3H, J=7Hz); 0.92 (d, 6H, J=7Hz).

According the same above described procedure and using the corresponding methyl ester of ketoprofen the following compound is obtained:

(R,S) 2-(3'-benzoylphenyl)-3-oxo-butyl, methyl-sulfoxide

¹H-NMR (CDCl₃); δ 7.85-7.60 (m, 4H); 7.52-7.40 (m, 5H); 3.80 (m, 2H); 3.55 (m, 1H); 2.62 + 2.55 (s, 3H); 2.47 (d, 2H, J=7Hz); 1.85 (m, 1H); 1.40 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

According the same above described procedure and using the methyl ester of the corresponding arylpropionic acids and methylsulfone (or phenylsulfone) instead of methylsulfoxide, the following compounds are obtained:

(R,S) 2-(4'-isobutylphenyl)-3-oxo-butyl, methyl-sulfone

¹H-NMR (CDCl₃); δ 7.18 (s, 4H); 4.18 (m, 2H); 3.90 (m, 1H); 3.10 (s, 3H); 2.40 (d, 2H, J=7Hz); 1.80 (m, 1H); 1.52 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

(R,S) 2-(3'-benzoylphenyl)-3-oxo-butyl, methyl-sulfone

¹H-NMR (CDCl₃); δ 7.85-7.60 (m, 4H); 7.52-7.40 (m, 5H); 4.20 (m, 3H); 3.95 (m, 1H); 3.18 (s, 3H); 1.55 (d, 3H, J=7Hz).

(R,S) 2-(3'-phenoxyphenyl)-3-oxo-butyl, methyl-sulfone

¹H-NMR (CDCl₃); δ 7.25-7.38 (m, 2H); 7.15-7.05 (m, 2H); 7.02 (m, 2H); 6.70-6.60 (m, 2H); 6.55 (s, 1H); 4.21 (m, 3H); 4.15 (m, 1H); 3.20 (s, 3H); 1.58 (d, 3H, J=7Hz).

(R,S) 2-(4'-isobutylphenyl)-3-oxo-butyl, phenyl-sulfone

¹H-NMR (CDCl₃); δ 8.05 (m, 2H); 7.75 (m, 1H); 7.60 (m, 2H); 7.15 (s, 4H); 4.15 (m, 2H); 3.95 (m, 1H); 2.40 (d, 2H, J=7Hz); 1.80 (m, 1H); 1.52 (d, 3H, J=7Hz); 0.94 (d, 6H, J=7Hz).

Example 12

5 (R)(-)-4-(4'-pyridyl)-2-[(4"-isobutyl)phenyl]butan-3-one

Diisopropylamine (0.17 mL; 1.21 mmol) and sodium hydride (60% in mineral oil, 0.106 mg; 2.66 mmol) are dissolved in dry THF (20 mL) under nitrogen atmosphere; 4-pyridylacetic acid (0.166 g; 1.21 mmol) is added portionwise to the mixture and the mixture refluxed for 15'. After cooling at T=0°-4°C by an ice-water bath, butyllithium (1.6 M in hexanes, 0.75 mL; 1.21 mmol) is added to the mixture and, after 30', a solution of R(-)-2-(4'-isobutylphenyl)propionyl chloride (0.27 g; 1.21 mmol) in dry THF (10 mL) is added dropwise. At the end of the adding, the ice-water bath is removed and the solution is left under stirring overnight at room temperature. The solvent is evaporated under reduced pressure and the residue is diluted with diethyl ether (20 mL), washed with water (3 x 15 mL), dried over Na₂SO₄ and evaporated under vacuum to give a dark red oil which is dissolved in 6N HCl (5 mL). The solution is heated at reflux for 2 hours; after cooling at room temperature the solvents are evaporated under vacuum and the residue is purified by flash chromatography to give pure R(-)-4-(4'-pyridyl)-2-[(4"-isobutyl)phenyl]butan-3-one (0.25 g; 0.88 mmol) as pale yellow oil.

20 [α]_D = -148° (c=1; CHCl₃). ¹H-NMR (CDCl₃); δ 8.54 (m, 2H); 7.15-6.90 (m, 6H); 3.85 (m, 1H); 3.72 (q, 2H, J=8 Hz); 2.51 (d, 3H, J=8Hz); 1.87 (m, 1H); 1.45 (d, 2H, J=7Hz); 0.92 (d, 6H, J=7Hz).

Example 13

(S) (+) dimethyl 3-(3'-phenoxy-phenyl)-2-oxo-butan-1-phosphonate.

25 Carbonyldiimidazole (0.18 g) is added to a solution of (S) 2-(3'-phenoxy-phenyl)-propionic acid (0.24 g) in anhydrous THF (5 mL) and is stirred for at least 1 h to form the corresponding imidazolid (Sol. A).

Separately, to a solution of dimethylphosphonoacetic acid (1.7 g) in anhydrous THF (25 mL) magnesium ethylate (0.5 g) is added, and the mixture is stirred for 3 h prior to rapid addition of the solution of imidazolid (Sol. A). The reaction mixture is stirred for 30 18 h at 25°C.

After evaporation of the solvent under vacuum, the residue is partitioned between ethyl acetate and 0.5 N aqueous HCl. The organic phase is washed with water, 5% aqueous sodium bicarbonate and water up to neutrality. After drying on Na₂SO₄, evaporation of the solvent and purification of the residue by flash chromatography on silica gel, 0.26 g of (S) (+) dimethyl 3-(3'-phenoxy-phenyl)-2-oxo-butyl-1-phosphonate are obtained.

[α]_D = +125° (c=1; CH₃OH); ¹H-NMR (CDCl₃); δ 7.25-7.32 (m, 2H); 7.15-7.05 (m, 2H); 7.03 (m, 2H); 6.70-6.65 (m, 2H); 6.50 (s, 1H); 4.15-3.9 (dd, 2H, J₁=15Hz, J₂=8Hz); 3.82 (s, 3H); 3.70 (m, 1H); 3.62 (s, 3H); 1.50 (d, 3H, J=8Hz).

Example 14

(R) 2-[4-(1-oxo-2-isoindoliny)phenyl]-3-oxo-valeramide

Carbonyldiimidazole (1.7 g) is added to a solution of 2.8 g of (R)-indoprofen in 15 mL of (anhydrous) THF, and is stirred for 2 h at room temperature to form the indoprofen imidazolide (Sol. A).

Separately, magnesium ethylate (2.3 g) is added, under stirring, to a solution of 4.2 g of the monoamide of malonic acid in 15 mL of THF. After the total dissolution of the reagents, the solution of the imidazolide is added, and the mixture is stirred for 24 h at room temperature.

After evaporation of the solvent under vacuum, the residue is divided between ethyl acetate and aqueous 0.5 N HCl. The organic phase is washed with water, 5% aqueous sodium bicarbonate and water up to neutrality. After drying on Na₂SO₄, evaporation of the solvent, and purification of the residue by flash chromatography on silica gel, 2.4 g of the amide of (R) 2-[4-(1-oxo-2-isoindoliny)phenyl]-3-oxo-valeric acid is obtained.

[α]_D = -46° (c=1; CH₃OH); ¹H-NMR (DMSO-d₆); δ 7.70-7.55 (m, 3H); 7.45-7.30 (m, 3H); 7.15 (d, 2H, J=8Hz); 5.55 (bs, 2H, CONH₂); 4.67 (s, 2H); 3.75 (m, 1H); 3.52 (s, 2H); 1.60 (d, 3H, J=8Hz).

Example 15

(R) 2-(4-(1-oxo-2-isoindoliny)phenyl)-3-oxo-valeronitrile.

Following the procedure of Example 14, and substituting the monoamide of malonic acid with equimolecular quantities of cyanacetic acid, (R) 2-(4-(1-oxo-2-isoindoliny)phenyl)-3-oxo-valeronitrile is obtained.

[α]_D = -21° (c=1; CH₃OH); ¹H-NMR (DMSO-d₆); δ 7.71-7.50 (m, 3H); 7.45-7.30 (m, 3H); 7.18 (d, 2H, J=8Hz); 4.65 (s, 2H); 3.72 (m, 1H); 3.63 (s, 2H); 1.55 (d, 3H, J=8Hz).

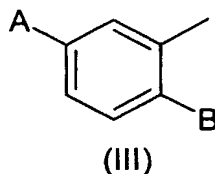
(*R, S*) (+)-2-butanone, 3-(3-benzoylphenyl);

ethyl (*R, S*) (+)-4-(3-benzoyl-phenyl)-3-oxo-pentanoate;

(*R,S*)(+)-1,3-dioxan-4, 6-dione-5-[2-(3-benzoylphenyl)-1-oxopropyl]-2,2-dimethyl.

2. Compounds according to Claim 1, wherein Ar represents phenyl, optionally substituted by one to three substituents, which are the same or different from one another, selected from:

halogens, C₁-C₄-alkyl, C₁-C₄-alkoxy, hydroxy, C₁-C₄-acyloxy, phenoxy, cyano, nitro, amino, C₁-C₄-acylamino, halogen-C₁-C₃-alkyl, halogen C₁-C₃-alkoxy, benzoyl, or a residue 4-isobutyl-phenyl, 3-benzoylphenyl, 5-benzoyl-2-acetoxy-phenyl, 3-phenoxy-phenyl, 5-benzoyl-2-thiophenyl, 4-thienoyl-phenyl, 1-oxo-2-isoindoliny-phenyl, 3-chloro-4-(2,5-dihydro-1H-pyrrol-1-yl)phenyl, 6-methoxy-β-naphthyl, 1-hydroxy-phenyl-1-methyl, or a residue of formula III:

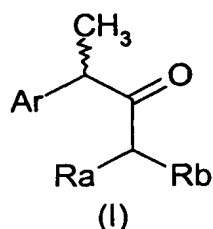


wherein A is benzyl, phenoxy, benzoyl, benzoyloxime, 1-hydroxy-phenyl-1-methyl, B is hydroxy, C₁-C₄-acyloxy or a group of formula -O-C(=S)-N(CH₃)₂, or -S-C(=O)-N(CH₃)₂.

3. Compounds according to Claim 2 wherein Ar is the residue 4-(2-methyl-propyl)-phenyl, 3-phenoxy-phenyl, 3-benzoylphenyl, -2-[4-(1-oxo-2-isoindoliny)phenyl], 5-benzoyl-thien-2-yl or 4-thienoyl-phenyl.

4. Compounds according to any one of Claims 1 to 3, wherein the steric configuration of the carbon atom to which the residue Ar is bound corresponds to the enantiomer (*R*).

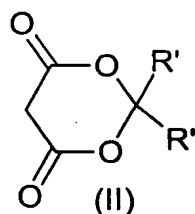
5. (*R,S*)-1-Arylethylketone compounds of formula I and their single (*R*) and (*S*) enantiomers:



wherein:

Ar is an aryl group;

Ra and Rb are independently chosen in the group of hydrogen, linear or branched C₁-C₆ alkyl, phenyl, α-or β-naphthyl, 2, 3, 4-pyridyl, C₁-C₄-alkylphenyl, C₁-C₄-alkyl(α-or β-naphthyl), C₁-C₄-alkyl(2, 3, 4-pyridyl), cyano (-CN), carboxamide, carboxyl or carboxyesters of formula CO₂R'' wherein R'' is the residue of a linear or branched C₁-C₆ aliphatic alcohol, a phosphonate PO(OR'')₂ wherein R'' is as defined above, a group of formula di-X-(CH₂)_n-Z, wherein X is a CO, SO, SO₂ group; Z is H, *tert*-butyl, isopropyl, CO₂R'', CN, phenyl, α-or β-naphthyl, 2, 3, 4-pyridyl, C₃-C₆ cycloalkyl, NH-BOC, NH₂; n is zero or an integer from 1 to 3; or Ra and Rb, with the carbon atom to which they are bound, form a cyclic residue 4, 6-dioxo-1, 3-dioxanyl-2, 2-disubstituted of formula II:



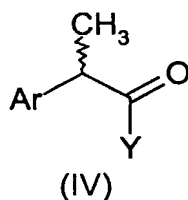
wherein R' is methyl or ethyl, or the two groups R' form a cyclohexane or cyclopentane ring;

for use as medicaments.

6. Compounds according to Claim 5 for use as inhibitors of IL-8 induced chemotaxis of human PMNs.

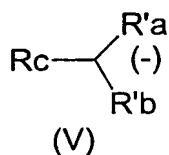
7. Pharmaceutical compositions containing a compound according to any one of Claims 1 to 6 in admixture with a suitable carrier thereof.

8. Use of the compounds according to any one of Claims 1 to 6 in the preparation of medicaments for the treatment psoriasis, rheumatoid arthritis, ulcerative colitis, acute respiratory distress syndrome (ARDS), idiopathic fibrosis, glomerulonephritis, bullous pemphigo and for the prevention and the treatment of damages caused by ischemia and reperfusion.
9. Process for the preparation of compounds according to any one of claims 1 to 6 comprising the reaction of an activated 2-arylpropionic acid of formula (IV)



wherein

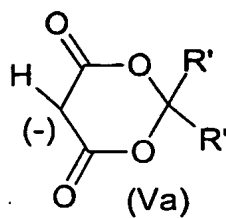
Ar is an aryl group and Y is a residue activating the carbonyl, such as halogen, 1-imidazolyl, pivaloyl, C₁-C₃-alkoxycarbonyl, succinyloxy, benzo-triazol-1-yloxy with a carbanion of formula V:



wherein:

- when R'a is the residue of a complex between a carboxyl and magnesium ethoxide, R'b is CO₂R'', CONH₂, CN, PO(OR'')₂ or -X-(CH₂)_n-Z', where X is as defined previously; R'c is H or -(CH₂)_n-Z', where Z' is H, *tert*-butyl, isopropyl, CO₂R'', CN, phenyl, α- or β-naphthyl, 2, 3, 4-pyridyl, C₃-C₆ cycloalkyl, NH-BOC;
- when R'a is hydrogen and R'c is hydrogen or a -(CH₂)_n-Z' radical, as defined above, R'b is phosphonate PO(OR'')₂, CO₂R'', or R'a and R'b with the carbon atom to which they are bound, form the carbanion of 2, 4-dioxo-1, 3-dioxanyl of formula Va:

25



wherein R' is methyl or ethyl, or the two groups R' form a cyclohexane or cyclopentane ring.

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